

shown in SEQ ID NOS:67-811.

34. (Twice Amended) The array of claim 32 wherein the open reading frame is identified by a SAGE tag selected from the group consisting of SEQ ID NOS:67, 68, 70, 71, 72, 83, 91, and 93.

Remarks

Applicants appreciate the Examiner's acknowledgement that the subject matter of claims 32-37, 43, and 44 meets the written description requirement of 35 U.S.C. § 112, first paragraph.

The Amendments to Claim 32

Claims 32 and 34 are amended to recite that the open reading frame "is identified by a SAGE tag" rather than "comprises a SAGE tag" This amendment is supported at page 6, lines 20-21: "New genes termed NORFs (not previously assigned open reading frames) have been found. They are uniquely identified by their SAGE tags."

This amendment is made so that claims 32 and 34 correctly reflect the fact that the SAGE tags that identify the NORFs can be located "either within or adjacent to intergenic ORFs." See the paragraph bridging pages 15-16. In fact, the particular open reading frames recited in claim 34 do not comprise the identifying SAGE tags. These amendments were not presented earlier because Applicants' representative realized that this correction needed to be made only after the Final Office Action was mailed. Claim 32 also is amended to delete an extraneous space after the word "cerevisiae."

The amendments do not narrow claims 32 or 34 or add new matter.

The Rejection of Claims 32-37, 43, and 44 Under 35 U.S.C. § 101

Claims 32-37, 43, and 44 remain rejected under 35 U.S.C. § 101. Applicants respectfully traverse this rejection.

In the response filed April 10, 2001, Applicants listed a number of utilities disclosed for the invention of claims 32-37, 32, and 44 in the specification. See page 7. The Final Office Action asserts that none of these utilities is a specific utility: "Any expressed DNA could be used for the same purposes; hence the uses are not specific to any one of the claimed embodiments." Final Office Action at page 2, fourth paragraph.

"Any expressed DNA," however, would not be useful on the claimed arrays. Most of the utilities disclosed for the claimed arrays in the specification require open reading frames that are involved in cell cycle progression:

- screening for drugs which affect cell cycle (*e.g.*, at page 2, lines 20-25);
- identifying human genes which are involved in cell cycle progression (*e.g.*, at page 3, lines 2-9, and at page 6, lines 17-19);
- marking phases of the cell cycle (*e.g.*, at page 6, lines 14-15); and
- generation of expression profiles of in response to drugs which affect cell cycle (*e.g.*, at page 9, lines 7-16).

Each of these utilities requires DNA that is differentially expressed during the cell cycle, as is the case for the disclosed NORFs. "Any" expressed DNA would not be useful for these embodiments, because "any" expressed DNA would not necessarily be differentially expressed during the cell cycle. Thus, the utilities disclosed in the specification for the NORFs recited in claims 32-37, 43, and 44 are specific.

Applicants respectfully request withdrawal of the rejection of claims 32-37, 43, and 44 under 35 U.S.C. § 101.

The Rejection of Claims 32-37, 43, and 44 Under 35 U.S.C. § 112, second paragraph

Claims 32-37, 43, and 44 remain rejected under 35 U.S.C. § 112, second paragraph, as allegedly indefinite. Applicants respectfully traverse this rejection.

The Final Office Action asserts that the claims are indefinite because the specification “does not disclose whether the SAGE tags mentioned in the claim[s] are contained in ORFs other than those in the tables.” It appears that the Final Office Action takes the position that, to be definite, the claims must specify that each of the recited SAGE tags can only identify one particular ORF. The specification teaches that this is the case at page 6, lines 20-21: “New genes termed NORFs (not previously assigned open reading frames) have been found. They are uniquely identified by their SAGE tags.” Because the specification teaches that the NORFs are uniquely identified by the recited SAGE tags, the meets and bounds of claims 32-37, 43, and 44 are clear.

Applicants respectfully request withdrawal of the rejection.

The Rejection of Claims 32-37, 43, and 44 Under 35 U.S.C. § 103(a)

Claims 32-37, 43, and 44 remain rejected under 35 U.S.C. § 103(a) as obvious over Goffeau *et al.* (*Science* 274, 546, 1996) in view of Velculescu *et al.* (*Science* 270, 484, 1995). Applicants respectfully traverse this rejection.

Goffeau *et al.* has been cited as disclosing the entire genome of *Saccharomyces cerevisiae*. Velculescu *et al.* has been cited as disclosing analysis of DNA by attaching DNA probes to a solid support. The Patent Office has asserted that it would have been obvious for the ordinary artisan to have combined the teachings of these two references and to have attached the DNAs of Goffeau *et al.* to the solid support of Velculescu *et al.* in order to analyze nucleic acid

sequences in *Saccharomyces cerevisiae*.

The Patent Office bears the burden of establishing a *prima facie* case of obviousness based on this combination of references. In particular, the combined references must teach or suggest all the claim limitations (M.P.E.P. § 706.02(j)). Moreover, the motivation to combine the cited references must be found in the references themselves or in the prior art. *Id.* The cited combination meets neither of these requirements.

The limitations of claims 32-37, 43, and 44 are as follows. Each of the claimed arrays must comprise at least one probe that comprises at least 14 nucleotides of a particular open reading frame of a *Saccharomyces cerevisiae* genome. The open reading frame is identified by a SAGE tag shown in SEQ ID NOS:67-811. Each of the claimed probe arrays must be present "on a solid support."

As Applicants have previously pointed out, none of the expressed open reading frames recited in claims 32-37, 43, and 44 are taught or suggested in either Goffeau *et al.* or Velculescu *et al.* In fact, the NORFs taught in the present specification were not even predicted to exist by previous analyses of the yeast genome. The open reading frames which Applicants refer to as "NORFS" ("not previously assigned open reading frames," page 6, line 20) are disclosed only in the present specification, not in the cited prior art.

The Final Office Action asserts that "[t]he claims contain open language, hence there is no need for the references to disclose any of the ORFs mentioned in the application." The specification teaches that the purpose of attaching an array of DNA probes to a solid support is to detect gene expression, *i.e.*, to hybridize mRNA (*e.g.*, page 8, lines 28). To analyze gene expression, *i.e.*, to detect *S. cerevisiae* mRNA, the DNA probes on the solid support must be capable of hybridizing to mRNA transcribed from expressed genes. The skilled artisan would

therefore not attach "any of the DNAs" of the *S. cerevisiae* genome to a solid support, but would attach probes which were known to be capable of hybridizing to mRNA, *i.e.*, probes from the elucidated open reading frames of the *S. cerevisiae* genome. As pointed out above, however, the open reading frames recited in claims 32-37, 43, and 44 were not previously known to be expressed. Thus, there would have been no motivation for the ordinary artisan to have attached DNA probes comprising all of the DNA of the *Saccharomyces cerevisiae* genome to a solid support.

Velculescu *et al.* does not teach attachment of DNA to a solid support for the purpose of detecting gene expression. Velculescu *et al.* discloses the technique known as "SAGE" (Serial Analysis of Gene Expression). The only teaching in Velculescu *et al.* of DNA attached to a solid support is at page 484, column 3, lines 10-12, where isolation of the most 3' portion of anchoring enzyme-cleaved cDNA is carried out by binding to streptavidin beads. This teaching would not have motivated an ordinary artisan to have placed DNA of *Saccharomyces cerevisiae* on a solid support to analyze gene expression.

The combination of Goffeau *et al.* and Velculescu *et al.* does not teach or suggest all the limitations of claims 32-37, 43, or 44, nor would the ordinary artisan have been motivated to combine these references. Thus, the Patent Office has failed to carry its burden of establishing that claims 32-37, 43, or 44 are *prima facie* obvious based on the cited references.

Applicants respectfully request withdrawal of this rejection of claims 32-37, 43, and 44 under 35 U.S.C. § 103(a).

Respectfully submitted,

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Appendix 1. Version of Amendments to the Claims with Markings to Show Changes Made

32. (Twice Amended) An array of probes on a solid support for detecting gene expression, wherein at least one probe comprises at least 14 contiguous nucleotides of an open reading frame of a *Saccharomyces* [*cerevisiae* ,] *cerevisiae*, wherein the *Saccharomyces* genome is shown in SEQ ID NOS:12,204-12,219, wherein the open reading frame is identified by [comprises] a SAGE tag as shown in SEQ ID NOS:67-811.

34. (Twice Amended) The array of claim 32 wherein the open reading frame is identified by [comprises] a SAGE tag selected from the group consisting of SEQ ID NOS:67, 68, 70, 71, 72, 83, 91, and 93.